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Dated 29 April 2003

Patents Form 1/77

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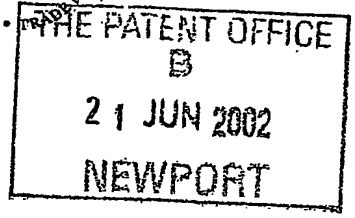

Request for grant of a patent

(See the notes on the back of this form. You can also get an explanatory leaflet from the Patent Office to help you fill in this form)

The Patent Office

Cardiff Road
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1. Your reference
   30057

2. Patent application number
   (The Patent Office will fill in this part)
   0214342.8
   21 JUN 2002

3. Full name, address and postcode of the or of each applicant *(underline all surnames)*
   Givaudan SA
   Chemin de la
   Parfumerie 5
   1214 Vernier
   Switzerland

   Patents ADP number *(if you know it)*
   8408031001

   If the applicant is a corporate body, give the country/state of its incorporation

4. Title of the invention
   Insect repellents

5. Name of your agent *(if you have one)*

   "Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*
   CIT Givaudan UK Ltd.
   Magna House
   76-80 Church Street
   Staines, Middleses TW18 4XR
   England

   Patents ADP number *(if you know it)*
   8408056001

6. If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or of each of these earlier applications and *(if you know it)* the or each application number

Country	Priority application number *(if you know it)*	Date of filing *(day / month / year)*

7. If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application

Number of earlier application	Date of filing *(day / month / year)*

8. Is a statement of inventorship and of right to grant of a patent required in support of this request? *(Answer 'Yes' if:*
   a) any applicant named in part 3 is not an inventor, or
   b) there is an inventor who is not named as an applicant, or
   c) any named applicant is a corporate body.
   See note (d))
   Yes

Patents Form 1/77

9. Enter the number of sheets for any of the following items you are filing with this form. Do not count copies of the same document

Continuation sheets of this form	
Description	20
Claim *(s)*	3
Abstract	1
Drawing *(s)*	

10. If you are also filing any of the following, state how many against each item.

Priority documents	
Translations of priority documents	
Statement of inventorship and right to grant of a patent *(Patents Form 7/77)*	
Request for preliminary examination and search *(Patents Form 9/77)*	1
Request for substantive examination *(Patents Form 10/77)*	
Any other documents *(please specify)*	

11. I/We request the grant of a patent on the basis of this application.

Signature [signature] Date 14/6/02

12. Name and daytime telephone number of person to contact in the United Kingdom

Colin Brown (Office time) Tel. 01 784417721

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Notes

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Insect repellents

The present invention relates to compounds having insect repellent characteristics and to compositions containing same.

Many insects are known as a nuisance and some insect genera even represent a health hazard. Therefore, many efforts have been made to eradicate or at least to control these pests. One method of insect eradication is through the use of synthetically produced insecticides. However, certain insect genera may develop resistance to some whilst others have undesirable effects on human and other animal life making their use highly regulated or even forbidden.

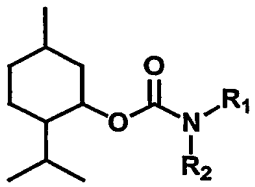
Naturally occurring substances are also known to display insect repellent properties, for example citronella oil, tolu and Peru balsams, camphor and various eucalyptus oils. However, many possess olfactory properties that makes their use in compositions that may usefully employing a perfume unacceptable, at least in amounts required to have repellent effects.

The prior art has continued to propose highly effective insect repellent compounds that have low, or substantially no odour. Thus, in US 5,182,305 N-aryl and N-cycloalkyl neoalkanamides are described. In US 5'391'578 N-lower alkyl neoalkanamides are described to be superior to DEET in long lasting effectiveness of the insect repellency. In WO 00/16738 menthyl 2-pyrrolidone-5-carboxylate is described to be an effective insect repellent, comparable to DEET. Finally, WO 02/15692 described compositions containing

certain menthane carboxamides having excellent insect repellent properties.

These prior art efforts reflect the consumer demand for improved insect repellent compounds that are not harmful to the user or the environment, and yet which are highly effective against target insect populations. Furthermore, as the end-uses of such compounds are in high-volume, low-price or commodity products, price sensitivity is an issue that has to be addressed in the development of new compounds.

Applicant has now found a new category of compounds having interesting insect repellent properties that meet the requirements set forth in the preceding paragraph. Thus the invention provides in a first aspect the use of a compound of the formula



wherein,

R_1 and R_2 are independently selected from the group consisting of H; an aliphatic residue having 1 to 20 carbon atoms, or a cycloaliphatic residue having 5 to 14 carbon atoms, or an aliphatic or cycloaliphatic residue aforementioned containing one or more hetero-atoms selected from O, N or S; an aryl or heteroaryl group having from 6 to 14 carbon atoms and wherein hetero-atoms are selected

from O, N or S; or any of the afore-mentioned groups substituted with a group selected from, C_{1-4} alkyl, C_{1-4} alkoxy, C_{2-4} alkenyl, aryl or heteroaryl as defined above, aryloxy, amino-, amido-, ester, keto-, hydroxyl, and halogen, e.g. Cl, Br or I, or

R_1 and R_2 together with the nitrogen atom to which they are attached form a 5- or 6-membered ring that may optionally contain additional hetero-atoms selected from O, N or S.

Preferred groups R_1 and R_2 may be selected from alkyl, e.g. C_{1-4} alkyl, more particularly methyl, ethyl, n or iso propyl, or n or sec butyl, cycloalkyl, e.g. having 5- or 6-carbon atoms or phenyl.

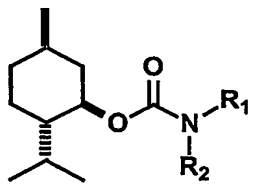
Most preferred groups R_1 and R_2 are those groups provided on the compounds of Example 1 hereinbelow.

The compounds n-butyl-carbamic acid (-)-menthyl ester; iso-butyl-carbamic acid (-)-menthyl ester; diethyl-carbamic acid (-)-menthyl ester; morpholine-4-carboxylic acid (-)-menthyl ester; and 3-[(-)-menthoxy-carbonylamino]-propionic acid ester have interesting insect repellent properties and these compounds form another aspect of the invention.

The compounds defined above display good repellent activity against insects, in particular against cockroaches. At the same they are safe to be applied to the human body, pets and livestock, or on or against surfaces which may be contacted by humans, pets or livestock. The compounds also possess good substantivity, thereby providing long-lasting activity against insect infestations on surfaces to which

they are applied. Furthermore, the compounds possess little or no odour, which makes them suitable for use in perfumed compositions.

The compounds of the invention have 3 chiral centres, giving rise to 8 stereoisomers. Thus, all possible stereoisomers are included in the scope of the present invention. However, in general, compounds having the stereo-chemistry set forth below



derived from the naturally occurring menthol [(-)3-p-menthanol] are preferred.

In a preferred embodiment of the present invention there is provided the use as an insect repellent of a compound or mixture of compounds selected from the compounds set forth in Example 1 below.

Compounds of the present invention may be prepared in a straight-forward manner. For example menthol may be reacted with a carbamoyl chloride bearing the groups R_1 and R_2 under basic conditions in a manner known in the art. The carbamoyl chlorides are either commercially available or can be synthesised from known starting materials according to synthetic procedures known to a person skilled in the

art. Alternatively, the readily available menthyl chloroformate may be reacted with an appropriate amine bearing the groups R_1 and R_2 to form compounds of the present invention, the amines bearing R_1 and R_2 being readily available.

Further and more specific information regarding the syntheses of the compounds is set forth in the Examples.

In another aspect of the present invention there is provided a composition comprising at least one of the compounds of the present invention as an insect repellent.

The amount of compound or compounds employed in said composition may vary widely depending on a number of factors including the nature of the insect infestation that is intended to be treated and the presence or absence of other insect repellent agents in the composition. Preferably however, a compound or mixtures of the compounds may be used at levels of from 1ppm to 1000ppm. Given the relatively low concentrations necessary for an insect-repellent effect, it might be preferable if the compound or mixture of compounds are provided at high concentrations, e.g. from 0.1 to 25% by weight of the composition, which can be diluted by the user to the desired concentration before use.

Compositions containing a compound or mixtures of compounds of the present invention may be applied to objects in need of protection against insects, either directly, in liquid solution or dispersion, as aerosols or air-sprays, or dispersed in a powdered carrier or in a suitable

composition. Compositions which may be useful to repel insects are, for example, detergent compositions, cleaning compositions, paints, wallpaper, upholstery and/or rug shampoos, liquid soaps, soap bars, floor polishes, floor waxes and furniture polishes. Compositions which are useful to repel insects from the human body are also included in the scope of the present invention and include compositions such as fine fragrances, colognes, skin creams, sun creams, skin lotions, deodorants, talcs, bath oils, soaps, shampoos, hair conditioners and styling agents.

The compositions of the present invention may comprise a compound or compounds of the present invention in combination with other known insect repellents, including, but not limited to, N,N-diethyl-m-toluamide (DEET), N,N-diethyl-benzamide, menthyl 2-pyrrolidone-5-carboxylate, N-aryl and N-cycloalkyl neoalkanamides, N-lower alkyl neoalkanamides and nepetalactone. The compositions of the present invention may also comprise natural oils known for their insect repellent characteristics. Examples for such oils include, without limiting, e.g. citronella oil, catnip oil, eucalyptus oil, cypress oil, galbanum oil, tolu and Peru balsams.

A compound of the present invention or mixtures thereof may also be used in conjunction with insecticides in order to repel insects from one area and toward the location, where the insecticide is applied to avoid the action of the insecticide in a special area, for example in areas containing foodstuffs.

A compound or mixtures of compounds of the present invention may be in admixture with fragrance compounds in compositions. Such fragrance compounds may be of natural and/or synthetic origin, examples for such natural and synthetic fragrance ingredients can be found e.g. in "Perfume and Flavour Materials of Natural Origin", S. Arctander, Ed., Elizabeth, N.J., 1960 and "Perfume and Flavour Chemicals", S. Arctander, Ed., Vol. I & II, Allured Publishing Corporation, Carol Stream, USA, 1994.

Additionally, or in the alternative, such compositions may contain solvents. Solvents that may be used are known to those skilled in the art and include, e.g. ethanol, ethylene glycol, propylene glycol, diethyl phthalate and dimethyl phthalate. As a preferred solvent dimethyl phthalate is used, which is known for its insect repellent characteristics.

The compositions of the present invention may comprise other ingredients normally used in the formulation thereof. Such ingredients are known to those skilled in the art and include e.g. anti-foaming agents, anti-microbial agents, anti-oxidants, anti-redeposition agents, bleaches, colorants, emulsifiers, enzymes, fats, fluorescent materials, fungicides, hydrotropes, moisturisers, optical brighteners, perfume carriers, perfume, preservatives, proteins, silicones, soil release agents, solubilisers, sugar derivatives, sun screens, surfactants, vitamins and waxes.

Compounds of the present invention have useful properties both as contact and vapour repellent. They are superior to

various commercial insect repellents in repelling action, especially against German cockroaches, which are considered to be one of the most difficult household pests to control. Due to their low vapour pressure the compounds are long-lasting on surfaces to which they have been applied. The long-lasting insect repellency may last up to 2-3 weeks after topical application depending on the concentration used. Furthermore, the compounds are sufficiently stable in compositions being object of the present invention to maintain their insect repellency.

Compositions of the present invention may also be incorporated in various materials during their manufacturing process. Methods for preparing a product comprising a composition according to the present invention by incorporating said composition into the product during extrusion are preferred.

Beside their effectiveness against German cockroaches, compounds of the present invention are also effective against other insects such as ants, bees, fleas, flies, hornets, mosquitoes, moths, silverfish, and wasps and against arachnids such as mites, spiders and ticks. The effectiveness against mosquitoes is important also due to economic reasons, especially against the genera Anopheles (which is a known carrier of malaria and transmits also filariasis and encephalitis), Culex (which is a carrier of viral encephalitis and filariasis) and Aedes (which carries yellow fever, dengue and encephalitis). From the latter genus, the activity against Aedes aegypti is especially important.

The invention will be further described, by way of illustration, in the following examples.

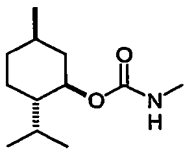
Example 1

General procedure for the synthesis of (-)-menthyl carbamates:

To a mechanically stirred solution of a corresponding amine (0.4 mol, 5 equiv.) in toluene (100 ml), cooled to 5 °C in an ice-water bath, was added dropwise a solution of (-)-menthyl chloroformate (17.5 g, 0.08 mol, 1 equiv.) in toluene (20 ml) within 0.5 h. The temperature was kept between 5 and 15 °C with cooling. The resulting suspension was allowed to warm to room temperature and stirring continued until the reaction was complete according to TLC analysis(0.5 to 3h).

The mixture was poured into ice/water (300 ml), extracted with toluene (2 x 200 ml) and the organic phases were each washed with aqueous hydrochloric acid (5%, 200 ml), water (200 ml) and brine (200 ml). The combined organic layers were dried over sodium sulphate and concentrated *in vacuo* to give the crude carbamate. (In the case of methylamine and ethylamine, where ethanolic solutions were used, the reaction mixture remains a solution and ethanol needs to be removed prior to aqueous work-up.) The crudes were either used without purification or purified by re-crystallisation from hexane or 'Kugelrohr' distilled to yield the clean (-)-menthyl carbamates in 75 to 90%.

Characterisation of (-)-menthyl carbamates:



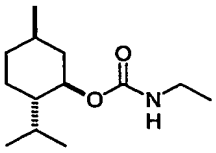
Methyl-carbamic acid (-)-menthyl ester

mp. 108-110 °C (hexane), white solid

^{1}H-NMR (400 MHz, $CDCl_3$, coupling constants in Hz): 0.79 (3H, d, *J* 7, Me); 0.80-0.98 (2H, m, 2 x CH); 0.89 (6H, d, *J* 7, Me_2); 1.06 (1H, dq, *J* 13, 4, CH); 1.29 (1H, brt, *J* 11, CH); 1.42-1.55 (1H, m, CH); 1.60-1.72 (2H, m, 2 x CH); 1.86-1.98 (1H, m, CH); 2.01-2.09 (1H, m, CH); 2.79 (3H, d, *J* 5, *Me*NH); 4.28-4.57 (1H, brm, NH); 4.55 (1H, dt, *J* 11, 4, CHOCO).

IR (ν_{max}, cm^{-1}, ATR): 3377w, 2961m, 1688s, 1525s, 1258s, 1139s.

MS [m/z (EI)]: 213 (M^+, <1%), 138 (70), 123 (41), 95 (100), 81 (73), 55 (56), 41 (47).



Ethyl-carbamic acid (-)-menthyl ester

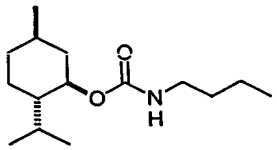
mp. 55-56 °C (hexane), white solid

^{1}H-NMR (400 MHz, $CDCl_3$, coupling constants in Hz): 0.79 (3H, d, *J* 7, Me); 0.81-0.99 (2H, m, 2 x CH); 0.89 (6H, d, *J* 7, Me_2); 1.05 (1H, dq, *J* 13, 4, CH); 1.13 (3H, t, *J* 7, CH_2*Me*); 1.28 (1H, brt, *J* 11, CH); 1.43-1.55 (1H, m, CH);

1.61-1.72 (2H, m, 2 x CH); 1.86-1.99 (1H, m, CH); 2.01-2.09 (1H, m, CH); 3.14-3.27 (2H, brm, CH_2NH); 4.26-4.65 (1H, brm, NH); 4.48-4.61 (1H, brm, CHOCO).

IR (ν_{max}, cm^{-1}, ATR): 3377w, 2960m, 1687s, 1524s, 1249s, 1019m.

MS [m/z (EI)]: 227 ($M+H^+$, <1%), 138 (65), 123 (28), 95 (100), 90 (83), 81 (82), 71 (41), 55 (57), 41 (32).



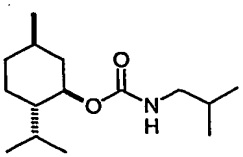
Butyl-carbamic acid (-)-menthyl ester

mp. 60-62 °C (hexane), white solid

^{1}H-NMR (400 MHz, $CDCl_3$, coupling constants in Hz): 0.79 (3H, d, *J* 7, Me); 0.80-0.98 (2H, m, 2 x CH); 0.89 (6H, d, *J* 7, Me_2); 0.92 (3H, t, *J* 7, CH_2Me); 1.06 (1H, dq, *J* 13, 4, CH); 1.28 (1H, brt, *J* 11, CH); 1.31-1.39 (2H, m, CH_2Me); 1.41-1.55 (3H, m, CH and CH_2); 1.61-1.72 (2H, m, 2 x CH); 1.87-1.98 (1H, m, CH); 2.00-2.09 (1H, m, CH); 3.11-3.23 (2H, brm, CH_2NH); 4.32-4.65 (1H, brm, NH); 4.48-4.61 (1H, brm, CHOCO).

IR (ν_{max}, cm^{-1}, ATR): 3369w, 2957m, 1686s, 1525s, 1240s, 1023m.

MS [m/z (EI)]: 138 ($M-HOCONHBu^+$, 26%), 123 (20), 118 (18), 95 (59), 81 (48), 71 (26), 56 (61), 41 (100), 27 (34).



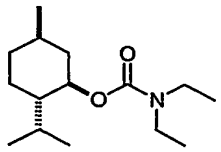
Isobutyl-carbamic acid (-)-menthyl ester

mp. 99-102 °C (hexane), white solid

^{1}H-NMR (400 MHz, $CDCl_3$, coupling constants in Hz): 0.79 (3H, d, *J* 7, Me); 0.80-0.98 (2H, m, 2 x CH); 0.89 (6H, d, *J* 7, Me_2); 0.90 (6H, d, *J* 7, Me_2); 1.06 (1H, dq, *J* 13, 4, CH); 1.28 (1H, brt, *J* 11, CH); 1.42-1.53 (1H, m, CH); 1.62-1.78 (3H, m, 3 x CH); 1.86-1.97 (1H, m, CH); 2.00-2.08 (1H, m, CH); 2.95-3.03 (2H, brm, CH_2NH); 4.45-4.68 (1H, brm, NH); 4.53 (1H, dt, *J* 11, 4, CHOCO).

IR (ν_{max}, cm^{-1}, ATR): 3373w, 2959m, 1687s, 1528s, 1276m, 1241s, 1144m, 1039m.

MS [m/z (EI)]: 138 (M-HOCONH*i*Bu$^+$, 28%), 123 (17), 118 (16), 95 (59), 81 (44), 71 (31), 56 (42), 43 (100), 27 (31).



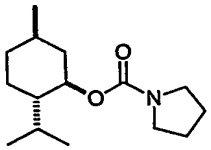
Diethyl-carbamic acid (-)-menthyl ester

bp. 90 °C, 0.03 mbar, colourless liquid

^{1}H-NMR (400 MHz, $CDCl_3$, coupling constants in Hz): 0.79 (3H, d, *J* 7, Me); 0.87 (1H, dt, *J* 11, 3, CH); 0.90 (6H, d, *J* 7, Me_2); 0.95 (1H, q, *J* 11, CH); 1.07 (1H, dq, *J* 13, 4, CH); 1.10 (6H, t, *J* 7, 2 x CH_2*Me*); 1.36 (1H, tt, *J* 11, 3, CH); 1.42-1.55 (1H, m, CH); 1.62-1.73 (2H, m, 2 x CH); 1.94 (1H, ddq, *J* 13, 7, 3, CH); 2.02-2.10 (1H, m, CH); 3.20-3.35 (4H, brm, 2 x CH_2NH); 4.57 (1H, dt, *J* 11, 4, CHOCO).

IR (ν_{max}, cm^{-1}, ATR): 2955m, 1695s, 1422m, 1271s, 1172s, 993m.

MS [m/z (EI)]: 255 (M^+, <1%), 138 (42), 118 (91), 95 (29), 83 (100), 69 (34), 55 (48), 41 (29).



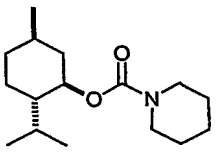
Pyrrolidine-1-carboxylic acid (-)-menthyl ester

crude product: colourless liquid

^{1}H-NMR (400 MHz, $CDCl_3$, coupling constants in Hz): 0.80 (3H, d, *J* 7, Me); 0.88 (1H, dt, *J* 11, 3, CH); 0.90 (6H, d, *J* 7, Me_2); 0.95 (1H, q, *J* 11, CH); 1.07 (1H, dq, *J* 13, 4, CH); 1.36 (1H, tt, *J* 11, 3, CH); 1.42-1.56 (1H, m, CH); 1.62-1.72 (2H, m, 2 x CH); 1.81-1.89 (6H, m, CH_2CH_2); 1.96 (1H, ddq, *J* 13, 7, 3, CH); 2.05-2.13 (1H, m, CH); 3.28-3.40 (4H, brm, 2 x CH_2NH); 4.55 (1H, dt, *J* 11, 4, CHOCO).

IR (ν_{max}, cm^{-1}, ATR): 2952m, 1699s, 1411s, 1100m.

MS [m/z (EI)]: 253 (M^+, <1%), 138 (31), 116 (100), 98 (26), 95 (38), 83 (65), 69 (29), 55 (61), 41 (32).



Piperidine-1-carboxylic acid (-)-menthyl ester

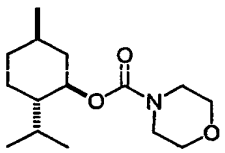
crude product: colourless liquid

^{1}H-NMR (400 MHz, $CDCl_3$, coupling constants in Hz): 0.79 (3H, d, *J* 7, Me); 0.88 (1H, dt, *J* 11, 3, CH); 0.91 (6H, d, *J* 7, Me_2); 0.94 (1H, q, *J* 11, CH); 1.07 (1H, dq, *J* 13, 4,

CH); 1.37 (1H, tt, *J* 11, 3, CH); 1.42-1.72 (9H, m, 3 x CH, $CH_2CH_2CH_2$); 1.92 (1H, ddq, *J* 13, 7, 3, CH); 2.03-2.10 (1H, m, CH); 3.40 (4H, t, *J* 6, 2 x CH_2NH); 4.55 (1H, dt, *J* 11, 4, CHOCO).

IR (ν_{max}, cm^{-1}, ATR): 2933m, 1695s, 1425m, 1231m.

MS [m/z (EI)]: 267 (M^+, <1%), 138 (41), 130 (100), 95 (43), 83 (66), 69 (41), 55 (47), 41 (46).



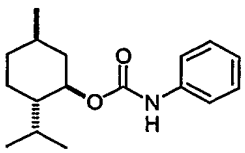
Morpholine-4-carboxylic acid (-)-menthyl ester

crude product: colourless liquid

^{1}H-NMR (400 MHz, $CDCl_3$, coupling constants in Hz): 0.79 (3H, d, *J* 7, Me); 0.87 (1H, dt, *J* 11, 3, CH); 0.90 (6H, d, *J* 7, Me_2); 0.95 (1H, q, *J* 11, CH); 1.08 (1H, dq, *J* 13, 4, CH); 1.36 (1H, tt, *J* 11, 3, CH); 1.42-1.56 (1H, m, CH); 1.63-1.72 (2H, m, 2 x CH); 1.89 (1H, ddq, *J* 13, 7, 3, CH); 2.03-2.11 (1H, m, CH); 3.46 (4H, t, *J* 5, 2 x CH_2NH); 3.65 (4H, t, *J* 5, 2 x CH_2O); 4.58 (1H, dt, *J* 11, 4, CHOCO).

IR (ν_{max}, cm^{-1}, ATR): 2956m, 1699s, 1420m, 1238s, 1117m.

MS [m/z (EI)]: 269 (M^+, <1%), 138 (61), 95 (42), 83 (100), 69 (37), 57 (41), 55 (53), 41 (33).



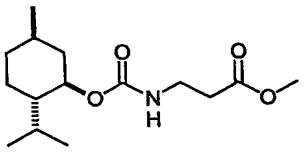
Phenyl-carbamic acid (-)-menthyl ester

mp. 111-113 °C (hexane), white solid

^{1}H-NMR (400 MHz, $CDCl_3$, coupling constants in Hz): 0.81 (3H, d, *J* 7, Me); 0.89 (1H, dt, *J* 11, 3, CH); 0.92 (6H, d, *J* 7, Me_2); 1.01 (1H, q, *J* 11, CH); 1.10 (1H, dq, *J* 13, 4, CH); 1.37 (1H, tt, *J* 11, 3, CH); 1.45-1.58 (1H, m, CH); 1.66-1.74 (2H, m, 2 x CH); 1.97 (1H, ddq, *J* 13, 7, 3, CH); 2.08-2.15 (1H, m, CH); 4.66 (1H, dt, *J* 11, 4, CHOCO); 6.54 (1H, brs, NH); 7.05 (1H, brt, *J* 7.5, PhH); 7.30 (2H, t, *J* 7.5, 2 x PhH); 7.38 (2H, brd, *J* 7.5, 2 x PhH).

IR (ν_{max}, cm^{-1}, ATR): 3364w, 2955m, 1697s, 1524s, 1443s, 1226s, 1050s.

MS [m/z (EI)]: 275 (M^+, 7%), 137 (28), 119 (89), 95 (84), 83 (100), 69 (45), 55 (82), 41 (62).



3-[(-)-menthoxy-carbonylamino]-propionic acid methyl ester

mp. 49-51 °C (hexane), white solid

^{1}H-NMR (400 MHz, $CDCl_3$, coupling constants in Hz): 0.79 (3H, d, *J* 7, Me); 0.80-0.98 (2H, m, 2 x CH); 0.91 (6H, d, *J* 7, Me_2); 1.05 (1H, dq, *J* 13, 4, CH); 1.29 (1H, brt, *J* 11, CH); 1.42-1.55 (1H, m, CH); 1.62-1.73 (2H, m, 2 x CH); 1.85-1.97 (1H, m, CH); 1.99-2.08 (1H, m, CH); 2.55 (2H, t, *J* 6, CH_2CO); 3.38-3.49 (2H, m, CH_2NH); 3.70 (3H, s, OMe); 4.53 (1H, dt, *J* 11, 4, CHOCO); 5.07-5.18 (1H, brm, NH).

IR (ν_{max}, cm^{-1}, ATR): 3362w, 2959m, 1734s, 1683s, 1530s, 1256s, 1199m, 1177s, 991m.

MS [m/z (EI)]: 286 ($M+H^+$, 3%), 148 (69), 138 (100), 123 (45), 116 (53), 104 (92), 95 (91), 81 (60), 55 (37), 41 (24).

Example 2:

The effectiveness of compounds of formula I as insect repellents is determined using German cockroaches exposed to a formica surface partially treated/partially untreated with a test compound of formula I.

The study was conducted in an air-conditioned laboratory at a temperature of 22°±2°C under a normal day/night cycle, using German cockroaches (*Blatella Germanica*) of mixed sex and age. The study was conducted over a 3 day period and the repellent effectiveness was assessed 1, 2 and 3 days after cockroach introduction.

Test method:

A. Treatment

One half of a rectangle of formica 40cm x 30cm was treated at 20 mg/m^2 of a test compound of formula I. This was achieved by soaking a paper wipe (Rag on a Roll ca 20cm x 20cm) in a solution of the test compound in ethanol, squeezing out the excess liquid and wiping over the surface to give the required coverage. This was checked by weighing the cloth after application. The surface was allowed to dry. The other half of the rectangle was wiped with ethanol alone (untreated surface).

B. Bioassays

The treated formica rectangle was placed on the bench

and a plastic container was placed on the rectangle. This had been treated with fluon to prevent cockroach escape.

Two sheets of formica (10cm x 10cm) were placed on the formica, one on the treated surface and one on the untreated surface. This acted as a cockroach harbourage. The formica sheet to be used in the treated section was treated at the same rate as the treated formica. The formica was placed on two 1cm high bottle tops to allow cockroaches access under the formica.

20 German cockroaches were added (5 adults and 15 nymphs) to the centre of the formica. No food and water was supplied for these cockroaches.

At 1, 2 and 3 days after cockroach introduction the number of cockroaches under each harbourage was counted. After each count the harbourage position was changed to avoid the possibility of habituation to one location, the harbourages were replaced and new cockroaches were added to replace any dead cockroaches.

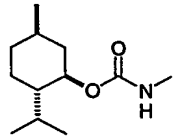
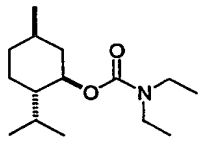
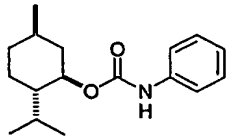
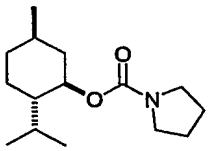
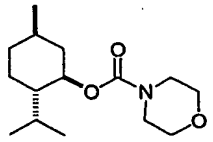
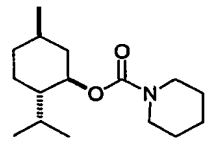
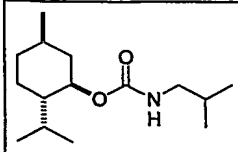
The above was repeated 3 times to provide a total of 4 replicates.

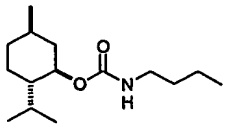
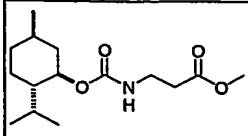
C. Repellency results for compound Methyl-carbamic acid (-)-menthyl ester

Time After Cockroach Introduction (Days)	Replicate	Number of Cockroaches present (n=20)			
		Treated Section	Untreated Section	Dead	Total
1	1	0	20	0	20
	2	0	19	1	20
	3	3	17	0	20
	4	1	19	0	20
	Total	**4**	**75**	**1**	**80**
2	1	1	19	0	20
	2	0	19	1	20
	3	0	20	0	20
	4	1	19	0	20
	Total	**2**	**77**	**1**	**80**
3	1	0	20	0	20
	2	0	20	0	20
	3	1	19	0	20
	4	0	20	0	20
	Total	**1**	**79**	**0**	**80**

Example 3

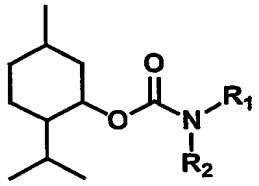
The methodology of Example 2 was repeated for all of the compounds set forth in Example 1. The results are presented in the table below.

Structure	Days after treatment	Percentage Present on	
Compound	Days after treatment	treated section	untreated section
	1	5.1	94.9
	2	2.5	97.5
	3	1.3	98.7
	Average	**3.0**	**97.0**
	1	7.6	92.4
	2	2.5	97.5
	3	2.5	97.5
	Average	**4.2**	**95.8**
	1	2.5	97.5
	2	3.7	96.3
	3	2.5	97.5
	Average	**2.9**	**97.1**
	1	2.5	97.5
	2	7.5	92.5
	3	12.7	87.3
	Average	**7.6**	**92.4**
	1	17.5	82.5
	2	17.5	82.5
	3	25.0	75.0
	Average	**20.0**	**80.0**
	1	10.0	90.0
	2	11.3	88.7
	3	3.9	96.1
	Average	**8.4**	**91.6**
	1	31.3	68.7
	2	17.5	82.5
	3	16.3	83.7
	Average	**21.7**	**78.3**

	1	6.3	93.7
	2	17.5	82.5
	3	7.5	92.5
	Average	**10.4**	**89.6**
	1	11.4	88.6
	2	2.5	97.5
	3	10.0	90.0
	Average	**8.0**	**92.0**

Claims

1. Use of a compound of the formula



wherein,

R_1 and R_2 are independently selected from the group consisting of H; an aliphatic residue having 1 to 20 carbon atoms, more preferably 1 to 6 carbon atoms, or a cycloaliphatic residue having 5 to 14 carbon atoms, or an aliphatic or cycloaliphatic residue aforementioned containing one or more hetero-atoms selected from O, N or S; an aryl or heteroaryl group having from 6 to 14 carbon atoms and wherein hetero-atoms are selected from O, N or S; or any of the afore-mentioned groups substituted with a group selected from, C_{1-4} alkyl, C_{1-4} alkoxy, C_{2-4} alkenyl, aryl or heteroaryl as defined above, aryloxy, amino-, amido-, ester, keto-, hydroxyl, and halogen, or

R_1 and R_2 together with the nitrogen atom to which they are attached form a 5- or 6-membered ring that may optionally contain additional hetero-atoms selected from O, N or S.

2. Use according to claim 1 wherein the compound is selected from the group consisting of

Methyl-carbamic acid (-)-menthyl ester;
Ethyl-carbamic acid (-)-menthyl ester;

Butyl-carbamic acid (-)-menthyl ester;
Isobutyl-carbamic acid (-)-menthyl ester;
Diethyl-carbamic acid (-)-menthyl ester;
Pyrrolidine-1-carboxylic acid (-)-menthyl ester;
Piperidine-1-carboxylic acid (-)-menthyl ester;
Morpholine-4-carboxylic acid (-)-menthyl ester;
Phenyl-carbamic acid (-)-menthyl ester; and
3-[(-)-menthoxy-carbonylamino]-propionic acid ester.

3. A compound selected from the group consisting of n-butyl-carbamic acid (-)-menthyl ester; iso-butyl-carbamic acid (-)-menthyl ester; diethyl-carbamic acid (-)-menthyl ester; morpholine-4-carboxylic acid (-)-menthyl ester; and 3-[(-)-menthoxy-carbonylamino]-propionic acid ester.

4. A composition comprising a compound as defined in any of the preceding claims in an insect-repellent amount.

5. A composition according to claim 4 wherein the compound is present in an amount from 1ppm to 25% bby weight.

6. Composition according to any of the claim 4 or 5 comprising one or more additional insect repellent.

7. Composition according to any of claims 4 to 6 comprising additionally one or more insecticides.

8. Composition according to any of the claims 4 to 7 comprising additionally a fragrance ingredient.

9. A product selected from the group consisting of a household product, an industrial cleansing product, a personal care product, or a pet or live-stock care

product comprising a compound or composition as defined in any of the preceding claims.

10. Fabrics and plastic materials comprising a composition or compounds as defined in any of the preceding claims.

11. Covering materials selected from floor, wall and furniture coverings comprising a compound or composition as defined in any of the preceding claims.

Abstract

The present invention relates to a composition having effective insect repellent characteristics comprising as an active ingredient an N-substituted p-menthane carboxamide, which has little or no odour and which is substantially non-toxic for human, pet and livestock